

REMARKS

Amendments

Claims 56-61, 64-68, 84-93, and 96-99 are currently pending in the application. Claims 62, 63, 69-83, 94, and 95 have been cancelled without prejudice or disclaimer solely to expedite patent prosecution in accordance with the U.S. Patent Office Business Goals (65 Fed. Reg. 54604 (September 8, 2000)). Applicants reserve the right to present the cancelled claims in a co-pending application.

Claims 56, 58, 84, and 85 have been amended for clarity, to correct minor typographical errors, and to more fully encompass Applicants' invention. In particular, independent claims 56 and 84 have been amended to recite:

- “and wherein a plurality of wells on the top surface of the cavitated wafer have a nucleic acid disposed therein” (see, *inter alia*, page 4, lines 10-12 of the originally filed specification); and
- “beads disposed within wells on the top surface” (see, *inter alia*, page 31, lines 21-22 and 28-29 of the originally filed specification).

Claim 84 has also been amended to recite “including sequential delivery of nucleotide triphosphates” (see, *inter alia*, page 5, lines 7-9 of the originally filed specification). Dependent claims 58 and 85 have been amended to recite “the diameter of each individual optical fiber in the cavitated wafer is between 6-50 μm ” (see, *inter alia*, page 36, lines 25-29).

Claims 57, 59-61, 64-68, 86-93, and 96-99 have been amended for clarity and to correct minor typographical errors. In particular, claim 57 has been amended to recite “immobilized on the wells or on said beads” (see, *inter alia*, Figure 1A and page 31, lines 21-22 and 28-29 of the originally filed specification). Claims 59-61 have been amended to recite “nucleic acids” (see, *inter alia*, page 10, line 17 of the originally filed specification). Claims 64-68 have been amended to recite “nucleic acid sequences” (see, *inter alia*, page 10, lines 18-22 of the originally filed specification). Claims 67-68 have been amended to recite “wells or beads” (see, *inter alia*, Figure 1A and page 31, lines 21-22 and 28-29 of the originally filed specification).

Applicants: Rothberg, et al.
U.S.S.N. 09/814,338

These amendments are supported by the application as originally filed, and do not constitute new matter. Specific support for the amendments is shown in parentheses, above. Entry of these amendments is respectfully requested.

Rejection under 35 U.S.C. §112, Second Paragraph

The Examiner has rejected claims 56-68, 84, 85, 87, and 90 under 35 U.S.C. §112, second paragraph, as allegedly indefinite for failing to particularly point out and distinctly claim the subject matter Applicants' regard as the invention (Office Action, pages 3-4). In particular, the Examiner has stated:

- Claim 56 and its dependents are considered indefinite for reciting a conjunction after its first element;
- Claim 57 is considered indefinite for recitation of the phrase "wherein the nucleic acid is an anchor primer";
- Claims 67 and 68 are considered indefinite for the recitation of the phrase "oligonucleotides are attached to the surface";
- Claim 84 is considered indefinite for recitation of the phrase "so nucleic acids disposed in the wells of the fiber optic wafer";
- Claim 85 is considered indefinite due to lack of an antecedent basis for the recitation of the phrase "said microparticle";
- Claim 87 is considered indefinite due to lack of an antecedent basis for the recitation of the phrase "said analyte"; and
- Claim 90 is considered indefinite due to lack of an antecedent basis for the recitation of the phrase "cavitated surface."

Claims 62-63 have been cancelled without prejudice or disclaimer as a result of this amendment (see above). In addition, Applicants have amended pending claims 56, 57, 67, 68, 84, 85, 87, and 90 for clarity. Specifically:

- Claim 56 has been amended to include recitation of "and" before the phrase "wherein a plurality of wells on the top surface of the cavitated wafer have a nucleic acid disposed therein" (see, *inter alia*, page 4, lines 10-12 of the originally filed specification);

- Claim 57 has been amended to recite “wherein the nucleic acid is immobilized on the substrate or on said beads” (see, *inter alia*, page 4, lines 5-7 and page 31, lines 21-22 and 28-29 of the originally filed specification);
- Claims 67 and 68 have been amended to recite “nucleic acid sequences are attached to the wells or beads by a linker” (see, *inter alia*, Figure 1A and page 31, lines 21-22 and 28-29 of the originally filed specification);
- Claim 84 has been amended to recite “so nucleic acids disposed on beads in the wells on the top surface of the fiber optic wafer” (see, *inter alia*, page 31, lines 21-22 and 28-29 of the originally filed specification);
- Claim 85 has been amended to delete the phrases “said microparticles” and “said microparticle”;
- Claim 87 has been amended to replace the phrase “said analyte” with “the nucleic acid,” which is supported by an antecedent basis; and
- Claim 90 has been amended to delete the recitation of “surface.”

These amendments are supported by the application as originally filed, and do not constitute new matter. It is believed that the amendments obviate this ground of rejection. Withdrawal of the rejection is respectfully requested.

Rejection under 35 U.S.C. § 102(a)

The Examiner has maintained the rejection of claims 73-78 under 35 U.S.C. §102(a), as allegedly being anticipated by Walt et al. (WO 98/50782) (Office Action, pages 4-5). In this Amendment, claims 73-78 have been cancelled without prejudice or disclaimer (see above). The claim cancellations obviate this ground of rejection. Withdrawal of the rejection is respectfully requested.

Rejection under 35 U.S.C. § 103(a) (Maintained)

The Examiner has maintained the rejection of claims 79-83 under 35 U.S.C. §103(a) as allegedly being unpatentable over Walt et al. (WO 98/50782) in light of Pantano et al. (*Chem. Mater.*, 8, pp. 2832-2835 (1996)) (Office Action, pages 5-6). In this Amendment, claims 73-83 have been cancelled without prejudice or disclaimer (see above). The claim cancellations obviate this ground of rejection. Withdrawal of the rejection is respectfully requested.

Rejection under 35 U.S.C. § 103(a) (New)

The Examiner has newly rejected claims 56-70, 72, and 84-99 under 35 U.S.C. §103(a) as allegedly being unpatentable over Walt et al. (US 2003/0027126; “Walt II”) (Office Action, pages 6-8). Applicants respectfully traverse this rejection.

On its face, the Walt II reference lists U.S. Patent Nos. 6,266,459 and 6,023,540 as priority documents. However, U.S. Patent Nos. 6,266,459 and 6,023,540 fail to teach or suggest the use of pyrophosphate sequencing reagent(s). The subject matter of “pyrophosphate sequencing” appears to have been specifically added the Walt II reference, which was filed on March 23, 2001. Applicants note that the filing date of Walt II falls *after* the filing date and priority date of the instant application. Because Walt II fails to teach or suggest the use of pyrophosphate sequencing reagent(s) prior to the filing or priority dates of the instant application, it cannot make obvious the claims of the instant application.

As presently amended, independent claims 56 and 84 recite the phrases “pyrophosphate sequencing reagent” and “pyrophosphate sequencing reagents,” respectively. Claims 57-61, 64-68, 88, 90, 92, and 93 of the instant application depend ultimately from claim 56. Claims 85-87, 89, 91, and 96-99 depend ultimately from claim 84. Therefore, all of the pending claims of the application include the subject matter “pyrophosphate sequencing reagent” or “pyrophosphate sequencing reagents.”

MPEP §2143.03 states that all of the claim limitations must be taught or suggested by the applied references to establish *prima facie* obviousness (citing *In re Royka*, 490 F.2d 981 (CCPA 1974)). Since Walt II did not teach or suggest the use of pyrophosphate sequencing reagents prior to the filing or priority dates of the instant application, a *prima facie* case of obviousness has not been established against pending claims 56-61, 64-68, 84-93, and 96-99 of the instant application. Applicants note that claims 62, 63, 69-83, 94, and 95 have been cancelled without prejudice or disclaimer (see above).

For all of these reasons, Applicants respectfully request withdrawal of this ground of rejection and reconsideration of instant claims 56-61, 64-68, 84-93, and 96-99.

In addition, Applicants respectfully wish to clarify certain aspects of the claimed invention. The Examiner has stated that Walt II fails to teach a cavitated fiber comprising a depth between 0.5 mm and 5.0 mm, and a polished end of a fiber optic wafer optically linked to a second fiber optic fiber (Office Action, page 7). The Examiner has also asserted that these aspects are obvious modifications of the reported system of Walt II, since they impart only ornamentation or portability (Office Action, pages 7-8). Although the Walt II reference does not make obvious the claimed invention for the reasons set forth above, Applicants wish to traverse this statement.

The claimed dimensions and detachable optical linkage of the wafer element of the instant application impart a notable advantage over the Walt II system. The Walt II system is not compatible for use with thermocyclers, due to its bulky housing and integrated microscope (see, e.g., Walt II, Figure 4). In contrast, the wafer element of instant claims 56-61, 64-68, 84-93, and 96-99 can be used with thermocycling machines because of its small size and detachable linkage. The instant application discloses that Applicants' methods and apparatuses can be employed for the sequencing of nucleic acids, and, specifically, for the sequencing of PCR products (see, *inter alia*, page 8, lines 20-30 to page 9, lines 1-5 of the originally filed specification). Inherently, the small size and detachable optic linkage of the wafer allows its insertion into thermocycling machines, and allows researchers to perform tandem PCR and sequencing reactions.

Thus, the claimed dimensions and detachable linkage are not merely aspects of ornamentation or portability, as characterized by the Examiner, but rather, highly advantageous features of Applicants' invention.

Provisional Double Patenting

The Examiner has maintained the provisional rejection of claims 56, 57, 64-67, 69, 70, 73, 74, 76, 77, 84, and 85 under 35 U.S.C. §101 as allegedly claiming the same invention as that of claims 33, 35, 41-44, 45, 46, 49-52, 59, and 60 of copending application U.S. Serial No. 90/664,197 (Office Action, page 9). It is noted that claims 69-83 of the instant application have been cancelled without disclaimer as a result of this Amendment. In addition, claims 34-48 and 52-58 have been cancelled without prejudice or disclaimer in the copending application. For pending claims 56, 57, 64-67, 84, and 85

Applicants: Rothberg, et al.
U.S.S.N. 09/814,338

of the instant application, Applicants respectfully request that this provisional rejection be held in abeyance until a claim has been allowed here or in the copending application.

Information Disclosure Statements

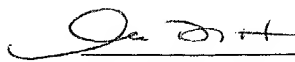
Applicants have submitted herewith a supplemental Information Disclosure Statement (IDS) under 37 C.F.R. §§1.56, 1.97, and 1.98, along with a Modified Form PTO-1449 and references listed on the form. In addition, Applicants have previously submitted an IDS, Modified Form PTO-1449, and references on February 1, 2002, as well as a supplemental IDS, Modified Form PTO-1449, and references on June 12, 2003. It is believed that all of these IDS submissions have complied with the requirements under 37 C.F.R. §§1.56, 1.97, and 1.98 and MPEP §609. MPEP §609 states that Examiners are required to consider all citations submitted in conformance with the IDS rules and MPEP requirements. In addition, a copy of the submitted Form PTO-1449 or other citation list, as reviewed and initialed by the Examiner, is to be returned to the Applicants with the next Office communication (MPEP §609). It is respectfully requested that the Examiner return to Applicants copies of all of the Modified Forms PTO-1449 that have been initialed to indicate that the cited information has been fully considered by the Patent Office during the examination of this application.

CONCLUSION

Applicants believe that the claims as amended are patentable and a prompt allowance is respectfully requested.

Dated: September 5, 2003

Respectfully submitted,


Ivor Elrifi, Reg. No. 39,529
Caryn DeHoratius Reg. No. 45,881
MINTZ, LEVIN, COHN, FERRIS,
GLOVSKY and POPEO, P.C.
The Chrysler Center
666 Third Avenue, 24th Floor
New York, NY 10017
Tel: (212) 935-3000
Fax: (212) 983-3115